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Assessment the role of survivin and FOXO1 in patient with acne vulgaris in Babylon City

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***Abstract*---**Acne is a chronic inflammatory disease of the pilosebaceous unit resulting from androgen-induced increased sebum production,occurs most prominently at skin sites with a high density of sebaceous glands such as the face,chest, and back. Survivin is an evolutionarily conserved eukaryotic protein that is essential for cell division , can inhibit cell death, Normally it is only expressed in actively proliferating cells. Survivin has been found to be increased in keratinocyte proliferative and inflammatory states, which are deeply involved in the pathogenesis of the acne lesions.Foxo1 is considered to be a representative member of the FoxO family, and has key transcription regulatory activities FoxOs are homeostatic factors in healthy skin and in skin disorders,Foxo1 a master regulatory factor for gluconeogenesis and glycogenolysis, as well as a positive regulator of the expression of insulin, is part of signaling axes related to the control of epidermal morphogenesis and the pathogenesis of acne ,The study was a case –control design which conducted in dermatology Al-Musayyab General Hospital and Al Imam Sadiq Hospital,Murjan Teaching Hospital. with 45 patients with Acne volgaris and 45 healthy controls, the level of serum survivin and Foxo1 were measured using an enzyme-linked immunosorbent assay (ELISA). AV patients had considerably higher serum survivin levels (243.13 ± 75.29ng/l) than normal controls (173.03 ± 87.62 ng/l) (p=0.000). Furthermore,Foxo1 levels in AV patients were considerably higher (4.74 ± 3.4 ng/ml). than in normal controls (2.37 ± 1.57)(p=0.0001). there were positive correlation between survivin and Foxo1 where p value is (<0.05), R (0.320). The serum survivin levels were statistically significant were compared according to gender, females had higher levels of survivin than the males (272.6±87.2 versus 219.5±55.3

ng/L, $p = 0.017$). as a result, Survivin and Foxo1 is a new biomarker that can be used to measure in AV patients.

***Keywords*---**acne volgaris, survivin, FOXO1.

Introduction

Acne vulgaris is a cutaneous chronic inflammatory disorder.[1] occurs due to increased sebum production, hypercornification of the pilosebaceous duct [2]. Acne vulgaris occurs in 79-95% of adolescents and young adults,Often, however, it develops in infants and children before adolescence.Under certain circumstances, especially when the symptoms of premature puberty or virilization coexist[3]. Hyperseborrhea has been considered as a major etiopathogenetic factor of acne. However, changes in sebaceous gland activity not only correlate with seborrhea but also with alterations in sebum fatty acid composition. [4]. As increased value is put on appearance, adolescents with acne may have a low quality of life with regard to their emotional state. Therefore, there is a high demand for an efficacious treatment for acne patients[5]. oxidative stress and inflammation set the stage for all subsequent pathogenic factors leading to acne[6] Acne vulgaris is classified based on patient age, lesion morphology (comedonal, inflammatory, mixed, nodulocystic), distribution (location on face, trunk, or both), and severity (extent, presence or absence of scarring, postinflammatory erythema, hyperpigmentation). Although most acne does not require specific medical evaluation, medical workup is sometimes warranted[7] acne is changes the skin distribution and severity over time, moreover, it can be a physically (scar development) and psychologically damaging condition that lasts for years[8]. Survivin (also known as BIRC5) is an evolutionarily conserved eukaryotic protein that is essential for cell division and can inhibit cell death. Normally it is only expressed in actively proliferating cells, When survivin (BIRC5) was first described, its discovery sparked considerable interest from oncologists and cell biologists, an interest that persists today. Survivin is a small protein [142 amino acids , 16.5 kDa] with multifunctional domains. Its N-terminal two-thirds comprise a globular baculovirus inhibitor of apoptosis repeat (BIR) domain (aa 20–90)[9]. Abnormal apoptosis and enhanced sebocyte survival mediated by survivin might affect infundibular keratinocyte differentiation and altered sebum production, leading to comedo formation and acne, and detect the relation of its levels with acne severity and presence of acne[10]. FoxOs is typically governed through post-translational modifications of the proteins, which, in turn regulate FoxOs subcellular localization and/or transcription different subtypes of FoxO proteins have different functions in different diseases. FoxO1 is localized on the nucleus, and it is expressed in all mammalian tissues including sebaceous glands[11]. FoxO1 is considered to be a representative member of the FoxO family, and has key transcription regulatory activities FoxOs are homeostatic factors in healthy skin and in skin disorders, An IGF1/FoxO1/p63 signaling axis regulates epidermal morphogenesis[12]. the Forkhead box protein O1 (FoxO1), a master regulatory factor for gluconeogenesis and glycogenolysis, as well as a positive regulator of the expression of insulin and of a series of circulating proteins that are involved in glucose counterregulation, such as the insulin growth factor binding protein 1 (IGFBP1), and the retinol binding protein 4

(RBP4)[13]. FoxO1 is part of signaling axes related to the control of epidermal morphogenesis and the pathogenesis of acne[14].

Materials and Method

Case-control study was used in this study. In the present report, 45 people with Acne volgaris were involved (25 males and 20 females) additionally to 45 healthy controls (25 males and 20 females) compatible with the Acne volgaris patients in age, sex, and body mass index (BMI). The mean age for AV males and females was 21.27 ± 3.19 and the mean age for healthy control males and females was 23.22 ± 3.42. A This study was done in private laboratories College of Medicine, University of Babylon , and the samples were collected from the registered attendances of the dermatology Clinic /Al-Musayyib General Hospital, Al-Imam Al-Sadiq Hospital, Murjan Teaching Hospital during the period from 1st of ganuary until 1st of june 2022. were estimated by sandwich ELISA technique.

Results

This study was showed most age of AV cases, was (15-30) years. The gender distribution of the studied groups was 45 patients with Acne volgaris, 25 (56.00%) male and 20 (44.00%) female, the results represented in figure (1).There was no significant difference in age (P=0.71) and BMI (P=0.56) between patients and control,The mean ± SD of Survivin levels for AV patients and control (243.13 ± 75.29, 173.03 ± 87.62 ng/L) respectively and P-value (0.000) as showed in table (1) & figure (2), and The mean ± SD of Foxo1 levels for AV patients and control (4.74± 3.4, 2.37 ± 1.57 ng /ml) respectively , P-value 0.001 as showed in table (1) & figure (3), The results show significant difference in level of survivin between male and female but no significant difference in level of Foxo1 between this subgroup, as shown in Table(2) The results show no significant difference in level of survivin, and Foxo1 between Mild&Sever, as shown in Table(3) & figure (4). The results show no significant difference in level of survivin, and Foxo1 between BMI subgroup, as shown in Table(4)

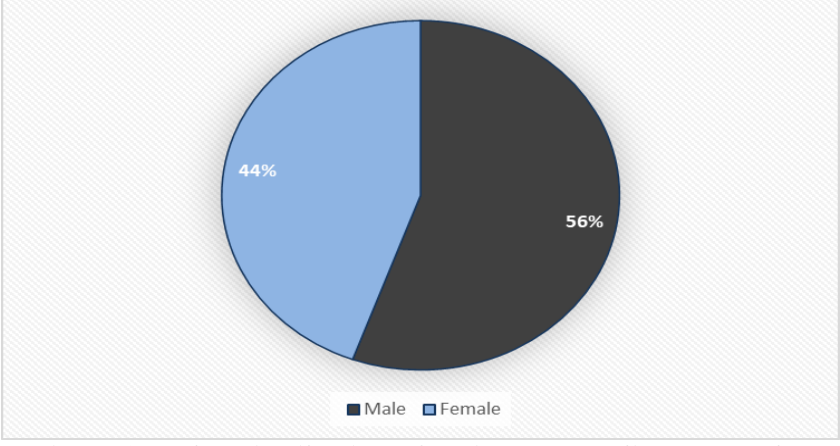


Figure (1): The Distribution of patients according to Gender

Table (1):Comparison of parameters (survivin),and (Foxo1) in patients and control groups

Parameter	group	N	Mean ± SD	p-value
survivin(ng\l)	control	45	173.03 ± 87.62	0.00 *
	patient	45	243.13 ± 75.29	
foxo1(ng\ml)	control	45	2.37 ± 1.57	0.001 *
	patient	45	4.74 ± 3.4	

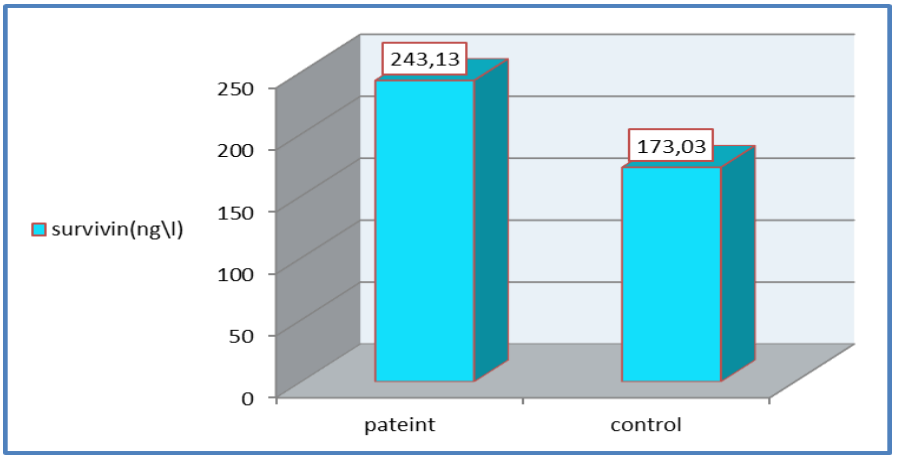


Figure (2) difference in survivin levels in AV patient & control

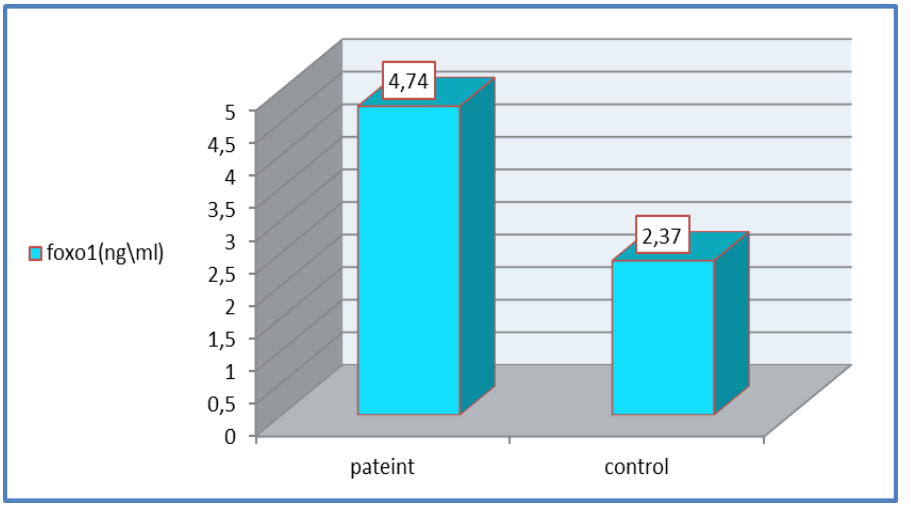


Figure (3) FOXO1 levels in acne vulgaris patient and control

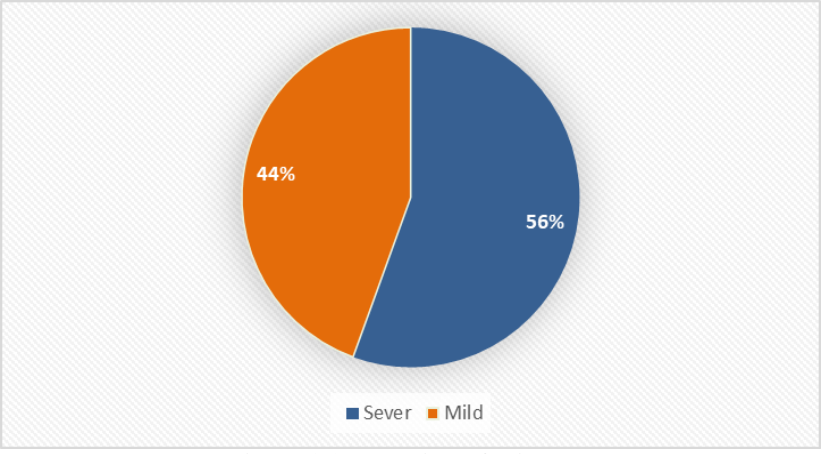
Table (2): Comparison of parameters (survivin),and (Foxo1) according to gender subgroup

Parameter	Gender subgroup	N	Mean ± SD	p-value
survivin(ng\l)	male	25	219.5 ± 55.3	

	Female	20	272.6 ± 87.2	**0.017 ***
foxo1(ng\ml)	male	25	3.88 ± 3.8	
	Female	20	5.82 ± 4.6	0.13

Table (3): Comparison of parameters (survivin),and (Foxo1) according to severity of disease

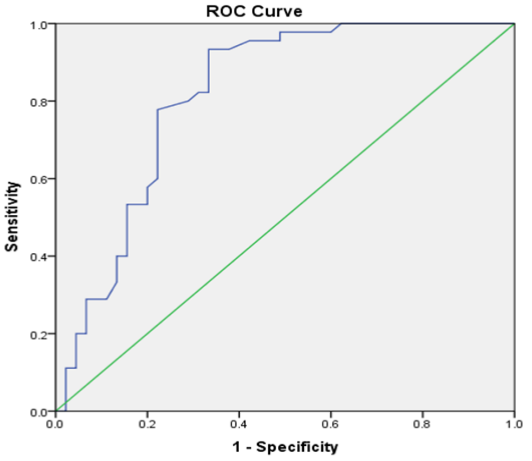
Parameter	Gender subgroup	N	Mean ± SD	p-value
survivin(ng\l)	Mild	20	223.9 ± 58.1	
	Sever	25	258.4 ± 84.6	0.12
foxo1(ng\ml)	Mild	20	4.1 ± 3.7	
	Sever	25	5.2 ± 4.6	0.42



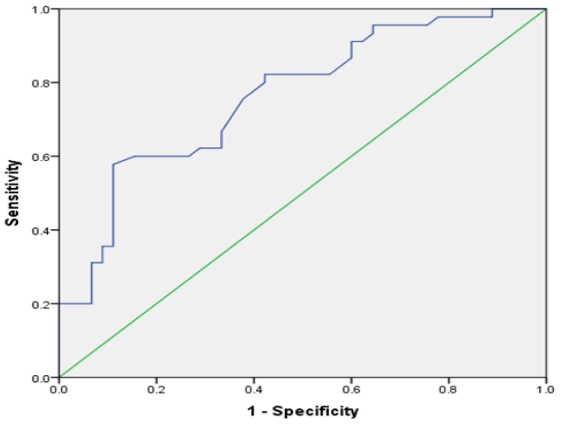
Figure(4) Severity of Disease

Table (4): Comparison of parameters (survivin),and (Foxo1) according to BMI subgroup

Parameter	BMI subgroup	N	Mean ± SD	p-value
survivin(ng\l)	normal weight	29	241.1 ± 82.4	
	over weight	16	246.7 ± 62.5	0.81
foxo1(ng\ml)	normal weight	29	4.98 ± 4.5	
	over weight	16	4.31 ± 3.9	0.62



Figure(5).Criterion values and coordinates of the ROC curve analysis for Survivin as differentiating patients from control subject



Figure(6).Criterion values and coordinates of the ROC curve analysis for Foxo1 as differentiating patients from control subject.

Discussion

this study showed that serum survivin levels were significantly increased in active acne and acne scar ($P<0.05$) groups in comparison to the healthy control group. These serum survivin levels were significantly higher in acne scar group and in the active acne group ($P<0.01$)[15] ,These findings support that there is a relationship between survivin and developing acne and acne scars. Moreover we found that there was statistical significant increase in survivin level among cases of active acne with progressive course compared to stationary cases ($P=0.001$)[16].When the serum survivin levels were compared according to gender, females had higher levels of survivin than the males [17].The cytoplasmic expression of FoxO1 was found to be significantly greater in the acne group, whereas in the control subjects this expression was likely to be nuclear. Excess consumption of a high-glycaemic-load diet was significantly associated with higher serum levels of cytoplasmic expression of FoxO1[18] FoxO1 functions as a

regulator in the pathogenesis of AV where FoxO1 integrates external and internal growth factors signals at the level of gene[19]. There was no significant correlation found between the genders in the control group for acne severity and mild [20]. There was no significant correlation between the Acne Volgaris and BMI. which was not significantly associated with BMI. [21]. In youths, overweight and obesity are inversely associated with acne in a dose-dependent manner . Overweight and obesity are associated with acne in girls aged 18 and 19, but the same association was not observed in boys. However, found no significant association between increased BMI and AV[22]. our result about relation agree with study.

Conclusion

Our findings suggest that Patients with AV had greater levels of Survivin and Foxo1 compare to healthy people indicates Survivin could be used as a prognostic marker in individuals with Acne volgaris to predict the development of acne scar.Also Foxo1 can be considered the main cause of Acne Volgaris.

Ethical Clearance

The Research Ethical Committee at scientific research by ethical approval of Both environmental and health and higher education and scientific research ministries in Iraq

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